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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,825	11/18/2003	Gregory Stephanopoulos	MIN-P01-042	7074
28120 7590 05/17/2007 FISH & NEAVE IP GROUP ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			EXAMINER STEELE, AMBER D	
			ART UNIT 1639	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/716,825

Applicant(s)

STEPHANOPOULOS ET AL.

Examiner

Amber D. Steele

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 October 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 8-32 is/are pending in the application.
- 4a) Of the above claim(s) 2-4 and 12-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 5-6, and 8-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f):
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 4/15/05.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application
- ☐ Other: _____.

DETAILED ACTION

1. The petition to revive the application after abandonment was granted on April 4, 2007.

Status of the Claims

2. The amendment received on October 2, 2006 canceled claim 7.

Claims 1-6 and 8-32 are currently pending.

Claims 1, 5-6, and 8-11 are currently under consideration.

Election/Restrictions

3. Applicant's election with traverse of Group I (old claims 1-11; now claims 1-6 and 8-11) in the reply filed on October 2, 2006 is acknowledged. The traversal is on the ground(s) that a serious search burden does not exist. This is not found persuasive because of the reasons of record in the Restriction requirement mailed on December 16, 2005 and due to the different classes and/or subclasses. In addition, applicants specifically requested that at least Group II be rejoined. However, Group II comprises limitations including notifying a patient, checking a patient's insurance policy, etc. that a search of the presently claimed method of utilizing gene expression to determine if a sample is positive for an oral disease would not be expected to overlap (e.g. patient could be notified in the office, patient's insurance policy has no relevance on diagnosis, etc.).

The requirement is still deemed proper and is therefore made FINAL.

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4. Claims 12-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Applicant timely traversed the restriction (election) requirement in the reply filed on October 6, 2006.

5. Applicant's election of mRNA as the species of expression level in the reply filed on October 6, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Please note: the species requirement for a species of a method of determining (B), species of gene (C), a species of tissue (D), and a species of oral disease (E) are withdrawn upon further consideration.

6. Claims 2-4 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on October 6, 2006.

Priority

7. The present application (10/716,825, filed November 18, 2003) claims status as a CIP of U.S. application 10/060,048 filed January 29, 2002 and claims benefit of U.S. provisional application 60/427,265 filed November 18, 2002.

8. The later-filed application must be an application for a patent for an invention, which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 10/060,048, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. U.S. application 10/060,048 does not teach HIV, tooth decay, gingivitis, pyorrhea, or periodontitis.

The disclosure of the prior-filed application, provisional Application No. 60/427,265, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. U.S. provisional application 60/427,265 does not teach tooth decay, pyorrhea, or periodontitis.

Therefore, the priority date for some limitations (i.e. tooth decay, pyorrhea, and periodontitis) of claim 11 is the present application filing date of November 18, 2003 and the priority date for some limitations of claim 11 (i.e. HIV and gingivitis) is November 18, 2002. All other claims presently have a priority date of January 29, 2002.

Information Disclosure Statement

9. The information disclosure statement (IDS) submitted on April 15, 2005 is being considered by the examiner.

Specification

10. The disclosure is objected to because of the following informalities: reference numbers 20 and 22 for Figure 2 are not described.

Appropriate correction is required.

11. The use of the trademark GeneChip® (please refer to pages 71 and 81) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

12. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Invention as Claimed

13. The presently claimed invention is drawn to a method for diagnosing an oral disease in a patient comprising: (a) obtaining a biological sample from a patient at the point of care, (b) determining the expression level of a plurality of genes associated with an oral disease in the biological sample, thereby producing a test expression profile, and (c) comparing the test expression profile with at least one signature expression profile of the plurality of genes indicative of an oral disease and variations thereof.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 1, 5-6, and 8-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 USC 112, first paragraph "Written Description" requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a **written description** rejection.

Claim 1 is drawn to a method for diagnosing an oral disease in a patient comprising (a) obtaining a biological sample from a patient at the point of care, (b) determining the expression level of a plurality of genes associated with oral disease (i.e. test expression profile), and (c) comparing the test expression profile with at least one signature expression profile. The invention as claimed encompasses all known genes associated with all oral diseases, all genes which may potentially be associated with all oral diseases in the future, and any yet to be discovered oral diseases. The claimed invention does not include any structural information regarding the genes.

The specification teaches 45 specific genes (please refer to Table 1). In addition, the specification teaches that of the various genes analyzed utilizing the GeneChip® array only 30 of the genes were “downregulated” and 15 of the genes were “upregulated” in five patients with oral cancer wherein the specific type of oral cancer is not disclosed (please refer to pages 69 and 72-73). However, the claimed invention does not include any structural limitations regarding the genes. Furthermore, the claimed invention does not teach how the genes can be utilized to diagnose oral disease (e.g. correlation of gene expression to disease; level of upregulation or downregulation expected in diseased samples, etc.). Therefore, one skilled in the relevant art would not reasonably conclude that the Applicants had possession of the invention as claimed since the structural limitations of the genes are not included in the claimed invention.

See Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was *in possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116.).

With the exception of the 45 gene names and oral cancer as disclosed by the specification, the skilled artisan cannot envision the method of claim 1. In addition, it is noted that while the art recognizes certain genetic markers that may correlate to oral diseases a specific, definitive genetic marker for diagnosing oral diseases including oral cancer have not been recognized in the art. For example, (1) Rosas et al. (Cancer Research 61: 939-942, 2001) teach that gene expression levels may not be altered, but rather methylation of the genes may be

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altered in head and neck tumors (i.e. only 23-56% of patients with head and neck primary tumors had hypermethylated genes; e.g. levels not conclusive for diagnostic purposes; please refer to abstract, Results, and Discussion sections), (2) Liao et al. (Oral Oncology 36: 272-276, 2000) teach that 62.5% of patients with oral squamous cell carcinoma were positive for p53 mutations while 18.52% of samples from healthy patients had p53 mutations (e.g. not conclusive for diagnostic purposes; please refer to abstract and Discussion section), and (3) Williams (Journal of Clinical Pathology 53: 165-172, 2000) teach that oral squamous carcinogenesis is a multistep process involving multiple genetic events wherein not all genetic events occur in all squamous oral carcinogenesis or similar genetic alteration may occur at different times (please refer to abstract and Conclusion section). Thus, while the art recognizes genetic markers that may correlate to oral diseases (e.g. associated with an oral disease or determining if a patient has a higher risk of having an oral disease), the art does not presently recognize one or more genetic markers that can be utilized to definitively diagnose oral diseases including oral cancer.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class wherein the specification provided only the bovine sequence.

16. Claims 1, 5-6, and 8-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a **scope of enablement** rejection.

There are many factors to consider when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any experimentation is “undue”. These factors include, but are not limited to:

1. The breadth of the claims;
2. The nature of the invention;
3. The state of the prior art;
4. The level of skill in the art;
5. The level of predictability in the art;
6. The amount of direction provided by the inventor;
7. The presence or absence of working examples;
8. The quantity of experimentation necessary needed to make or use the invention

based on the disclosure.

See *In re Wands* USPQ 2d 1400 (CAFC 1988):

The breadth of the claims and the nature of the invention:

The presently claimed invention is drawn to a method for diagnosing an oral disease in a patient comprising: (a) obtaining a biological sample from a patient at the point of care, (b) determining the expression level of a plurality of genes associated with an oral disease in the biological sample, thereby producing a test expression profile, and (c) comparing the test expression profile with at least one signature expression profile of the plurality of genes

indicative of an oral disease and variations thereof. The present claims do not provide any structural limitations regarding the genes utilized in the method, do not limit the type of oral disease, and do not provide any structural information regarding the expression profiles (i.e. test or signature). Accordingly, the claims encompass all known and unknown genes, all known and unknown oral diseases, and all known and unknown expression profiles. While the presently claimed method is enabled for screening biological samples for gene expression, the intended use as a means for diagnosing oral diseases is not enabled. The present specification merely states that of the various genes analyzed via GeneChip® array, the samples from five oral cancer patients (type, stage, etc. not specified) varied in 45 genes wherein 30 genes were “downregulated” and 15 of genes were “upregulated” (please refer to pages 69 and 72-73). The specification does not provide information regarding the level of upregulation or downregulation compared to control (e.g. normal, noncancerous sample). Accordingly, the claim scope is unduly broad with respect to encompassed genes, oral diseases, and expression profiles.

The state of the prior art and the level of predictability in the art:

Diagnosis of oral diseases via altered gene expression is highly unpredictable, particularly in humans. Rosas et al. (Cancer Research 61: 939-942, 2001) teach that gene expression levels may not be altered, but rather methylation of the genes and only 23-56% of patients with head and neck primary tumors had hypermethylated genes (e.g. levels not conclusive for diagnostic purposes; please refer to abstract, Results, and Discussion sections). Liao et al. (Oral Oncology 36: 272-276, 2000) teach that 62.5% of patients with oral squamous cell carcinoma were positive for p53 mutations while 18.52% of samples from healthy patients had p53 mutations (e.g. not conclusive for diagnostic purposes; please refer to abstract and

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Discussion section). Furthermore, Williams (Journal of Clinical Pathology 53: 165-172, 2000) teach that oral squamous carcinogenesis is a multistep process involving multiple genetic events wherein not all genetic events occur in all squamous oral carcinogenesis or similar genetic alteration may occur at different times (please refer to abstract and Conclusion section). Therefore, the level of predictability in the art is dependent on many factors including data interpretation, statistical analysis, animal models (e.g. wherein animal knockouts could provide more definitive evidence), long-term studies (e.g. following patients throughout course of disease to determine if gene expression is altered), etc. While finding genetic markers to accurately diagnose oral diseases is important, the state of the art requires vast amounts of data including correlation of the gene to disease with high probability, potentially finding one or more genetic markers for each oral disease, detailed statistical analysis of data, etc.

The level of skill in the art:

The level of skill would be high, most likely at the Ph.D. level.

The amount of direction provided by the inventor and the existence of working examples:

There are no specific examples directed to the intended use language of the presently claimed invention (i.e. diagnosing oral disease in patients), nor is there any information provided regarding correlating the altered gene expression data provided in the specification and diagnosing oral diseases. The specification contains only cursory statements that various genes are “down” or “up” in cancer (please refer to Table 1).

The quantity of experimentation needed to make or use the invention based on the content of the disclosure:

In light of the unpredictability surrounding the claimed subject matter, the undue breadth of the claimed invention's intended use, and the lack of adequate guidance, one wishing to practice the presently claimed invention would be unable to do so without engaging in undue experimentation. One wishing to practice the presently claimed invention would have to facilitate clinical studies with large numbers of patients suffering from each known oral disease and screen the entire genome to determine if any genes may be correlated to disease, follow patients for years to determine if gene expression changes during the course of the disease, provide detailed statistical analysis of the data to limit potential false positives/negatives, etc.

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 1, 5-6, and 8-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of ordinary skill in the art would not be able to determine the scope of the presently claimed invention. The terms "point of care" and "signature expression profile" are indefinite. For example, if a dentist or other practitioner requests the patient to go to another facility to have the sample drawn (e.g. hospital, phlebotomist's office, laboratory, etc.) is this still the "point of care", does the sample have to be taken at a reactionary's office, does another sample have to be taken if the patient is referred to a specialist, etc.? For example, is a signature expression profile from a patient known to have an oral disease, a "normal" donor, etc.; does the signature expression profile have 1, 2, 4, 8, 16, 32, etc. genes; etc.?

19. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of ordinary skill in the art would not be able to determine the scope of the presently claimed invention. It is unclear how assaying biological samples including bone marrow aspirates, bone marrow biopsies, lymph node aspirates, and lymph node biopsies would be useful in diagnosing oral diseases. For example, does the oral disease (i.e. cancer) have to be metastatic in order for these samples to provide useful diagnostic information, etc.?

20. Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. . One of ordinary skill in the art would not be able to determine the scope of the presently claimed invention. HIV is not art recognized as an oral disease (please refer to Levy ed., HIV and the Pathogenesis of AIDS, 1998, page 26; Truelove et al. JADA 126: 1394-1399, 1995). For example, is the oral disease caused by the immunosuppression related to HIV infection (e.g. opportunistic infection), etc.?

Claim Rejections - 35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

22. Claims 1, 5-6, and 8-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillman et al. U.S. 6,121,019 issued September 19, 2000.

For present claim 1, Hillman et al. teach methods of correlating genetic markers to disease comprising obtaining a biological sample (e.g. at "point of care"), determining the expression levels of genes, and comparing the sample expression levels to controls (e.g. signature expression profile; please refer to the entire specification particularly column 1, lines 10-15; column 2, lines 4-9; columns 11-20 and 28-33: Examples I-XII). Regarding the limitation that the sample must be obtained at the "point of care", the Office does not have the facilities and resources to provide the factual evidence needed in order to determine if the samples taught by Hillman et al. were obtained at the point of care. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the samples are different from the ones taught by the prior art and to establish the patentable differences. Please refer to see *in re Best* 562F.2d 1252, 195 U. S. P. Q. 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ2d 1922 (PTO Bd.Pat. App. & Int. 1989).

For present claim 5, Hillman et al. teach detecting mRNA levels (please refer to the entire specification particularly column 6, lines 57-67; column 9, lines 1-5; Example IV).

For present claim 6, Hillman et al. teach isolation of nucleic acids from the samples (please refer to the entire specification particularly Example I).

For present claim 8, Hillman et al. teach salivary gland cancer (e.g. oral cancer) and microarrays comprising 8, 24, 96, 384, 1536, or 6144 dots (e.g. genes; please refer to the entire specification particularly column 22, lines 1-16; column 29, lines 19-29; Example VII).

For present claim 9, Hillman et al. teach salivary gland cancer (e.g. oral cancer) and three genes including HCDR-1, HCDR-2, and HCDR-3 (e.g. subset; please refer to the entire specification particularly columns 2-5; column 22, lines 1-16; column 29, lines 19-29).

For present claim 10, Hillman et al. teach samples including tissue and body fluids (please refer to the entire specification particularly column 10, lines 49-55).

For present claim 11, Hillman et al. teach salivary gland cancer (e.g. oral cancer; please refer to the entire specification particularly column 22, lines 1-16; column 29, lines 19-29).

Therefore, the presently claimed invention is anticipated by the teachings of Hillman et al.

23. Claims 1, 5-6, and 8-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Katz et al. U.S. Patent 6,797,471 filing date of August 6, 2001 and effective filing date of August 4, 2000.

For present claim 1, Katz et al. teach methods of identifying a subject at risk for developing smoking related cancers including obtaining a biological sample (e.g. point of care), determining expression levels of genes, and comparing to controls (e.g. signature expression profile; please refer to the entire specification particularly abstract; Figures 1-2 and 10-12; columns 3-6 and 8-21; claims 1-21). Regarding the limitation that the sample must be obtained at the "point of care", the Office does not have the facilities and resources to provide the factual

evidence needed in order to determine if the samples taught by Katz et al. were obtained at the point of care. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the samples are different from the ones taught by the prior art and to establish the patentable differences. Please refer to see *in re Best* 562F.2d 1252, 195 U. S. P. Q. 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ2d 1922 (PTO Bd.Pat. App. & Int. 1989).

For present claim 5, Katz et al. teach determining mRNA expression (please refer to the entire specification particularly column 16, lines 32-40; column 18, lines 35-54).

For present claim 6, Katz et al. teach isolating nucleic acids from the samples (please refer to the entire specification particularly column 14, lines 66-67; column 15, lines 1-4).

For present claim 8, Katz et al. teach mouth cancer, genes from chromosomes 3 and 10 particularly sections 3p21.3 and 10q22, genomic libraries, biomarkers, arrays, chips (e.g. over 45 genes; please refer to the entire specification particularly column 3, lines 1-28; column 5, lines 50-60; column 6, lines 6-25; column 11, lines 10-67; column 12, lines 59-67; column 13; column 19, lines 55-67; columns 20-21).

For present claim 9, Katz et al. teach mouth cancer and genes including RPL14, CD39L3, PMGM, GC20, and PTEN (e.g. subset; please refer to the entire specification particularly column 3, lines 1-28; column 4, lines 37-46; column 6, lines 6-25).

For present claim 10, Katz et al. teach biological samples including tissue and fine needle aspirations (please refer to the entire specification particularly column 3, lines 21-28; column 14).

For present claim 11, Katz et al. teach mouth cancer (please refer to the entire specification particularly column 3, lines 14-28; column 6, lines 6-25).

Therefore, the presently claimed invention is anticipated by the teachings of Katz et al.

24. Claims 1, 5-6, and 8-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Warrington et al. U.S. Patent 7,108,969 filing date of September 10, 2001 and effective filing date of September 8, 2000.

For present claim 1, Warrington et al. teach methods for monitoring gene expression profiles associated with oral cancer comprising obtaining a biological sample, determining (e.g. point of care), determining expression levels of genes, and comparing to controls (e.g. signature expression profile; please refer to the entire specification particularly abstract; Figures 1A, 1B, 2A, 2B, 2C, 3-6, 7A-7K; columns 2-13; Examples I-IV; claims 1-19). Regarding the limitation that the sample must be obtained at the "point of care", the Office does not have the facilities and resources to provide the factual evidence needed in order to determine if the samples taught by Warrington et al. were obtained at the point of care. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the samples are different from the ones taught by the prior art and to establish the patentable differences. Please refer to see *in re Best* 562F.2d 1252, 195 U. S. P. Q. 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ2d 1922 (PTO Bd.Pat. App. & Int. 1989).

For present claim 5, Warrington et al. teach determining mRNA expression (please refer to the entire specification particularly column 6, lines 31-54; column 7, lines 29-43; Example II).

For present claim 6, Warrington et al. teach isolation of nucleic acids from samples (please refer to the entire specification particularly column 7, lines 29-43; Example I).

For present claim 8, Warrington et al. teach oral cancer, 56 genes which are upregulated or downregulated, more than 45 genes, and microarrays (please refer to the entire specification particularly Figures 2C, 2D, and 7A-7K; column 2; Example II).

For present claim 9, Warrington et al. teach oral cancer, 39 genes, gene subsets (please refer to the entire specification particularly Figures 2A, 2B, 2C, 2D, 6, 7A-7K; column 2).

For present claim 10, Warrington et al. teach biological samples including tissue, blood (e.g. serum), and fine needle biopsy (e.g. aspirates; please refer to the entire specification particularly column 7, lines 29-57).

For present claim 11, Warrington et al. teach oral cancer (please refer to the entire specification particularly column 2; Example I).

Therefore, the presently claimed invention is anticipated by the teachings of Warrington et al.

Future Communications

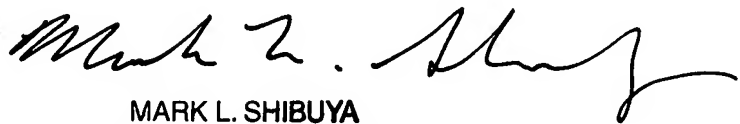
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ADS
May 9, 2007



MARK L. SHIBUYA
PRIMARY EXAMINER